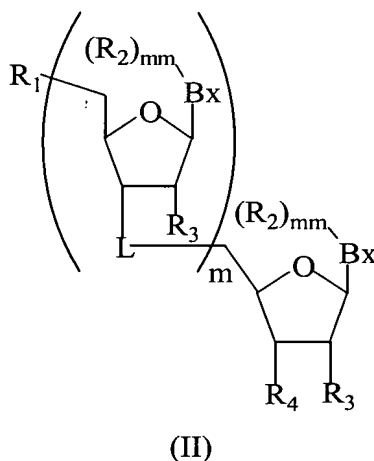


This listing of claims will replace all prior versions, and listings, of claims in the application.

**Listing of Claims:**

1 - 32. (Withdrawn).

33. (Currently amended) A compound of formula II:



wherein:

each Bx is an optionally protected heterocyclic base moiety;

R<sub>1</sub> is hydrogen, hydroxyl, a protected hydroxyl, a nucleoside, a nucleotide, an oligonucleoside, an oligonucleotide or a group of formula I;

R<sub>4</sub> is hydrogen, hydroxyl, a protected hydroxyl, a nucleoside, a nucleotide, an oligonucleoside, an oligonucleotide or a group of formula I;

each R<sub>2</sub> is a group of formula I:



(I)

wherein:

each n is, independently, from 1 to about 10;

each J is, independently, a sulfonic acid (-S(=O)<sub>2</sub>OH), a sulfonate salt (-S(=O)<sub>2</sub>O<sup>-</sup>X<sup>+</sup>), a sulfoxide (-S(=O)-Z), a sulfone (-S(=O)<sub>2</sub>-Z), -SH, -S-S-Z, or a thiol (-S-Z);

each X<sup>+</sup> is a metal cation;

each Z is, independently, selected from the group consisting of C<sub>1</sub>-C<sub>20</sub> alkyl, C<sub>2</sub>-C<sub>20</sub> alkenyl, C<sub>2</sub>-C<sub>20</sub> alkynyl, C<sub>5</sub>-C<sub>20</sub> aryl and C<sub>5</sub>-C<sub>20</sub> aryl substituted C<sub>1</sub>-C<sub>20</sub> alkyl;  
each R<sub>3</sub> is, independently, hydrogen, hydroxyl, a protected hydroxyl, an optionally protected sugar substituent group or a group of formula I;  
L is an internucleoside linking group;  
m is from 3 to about 50; and  
each mm is, independently, 0 or 1;  
wherein at least one of said L is other than a phosphodiester internucleoside linkage and at least one of said R<sub>1</sub>, R<sub>2</sub>[[, R<sub>3</sub>]] and R<sub>4</sub> is a group of formula I.

34. (Original) The compound of claim 33 wherein at least one R<sub>3</sub> is an optionally protected sugar substituent group.

35. (Original) The compound of claim 33 wherein at least two of said R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, and R<sub>4</sub> are groups of formula I.

36. (Original) The compound of claim 35 wherein at least two of said R<sub>3</sub> are, independently, groups of formula I.

37. (Original) The compound of claim 33 wherein substantially all R<sub>3</sub> are groups of formula I.

38. (Original) The compound of claim 33 wherein R<sub>1</sub> is a group of formula I.

39. (Original) The compound of claim 33 wherein R<sub>4</sub> is a group of formula I.

40. (Original) The compound of claim 33 wherein J is -S-Z and Z is a straight or branched C<sub>1</sub> to C<sub>20</sub> alkyl group.

41. (Original) The compound of claim 40 wherein said alkyl group is methyl, ethyl or propyl.

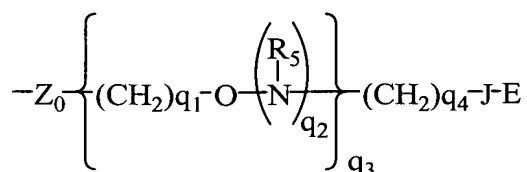
42. (Original) The compound of claim 41 wherein said alkyl group is methyl.
43. (Original) The compound of claim 33 wherein J is -S-Z and Z is aryl having from 5 to about 14 carbon atoms.
44. (Original) The compound of claim 33 wherein Z is phenyl.
45. (Original) The compound of claim 33 wherein at least one J is a sulfonic acid.
46. (Original) The compound of claim 33 wherein at least one J is a sulfonate salt.
47. (Original) The compound of claim 46 wherein  $X^+$  is  $Na^+$ .
48. (Original) The compound of claim 33 wherein at least one J is a sulfoxide.
49. (Original) The compound of claim 48 wherein Z is substituted or unsubstituted  $C_1$ - $C_{20}$  alkyl or substituted or unsubstituted  $C_5$ - $C_{20}$  aryl.
50. (Original) The compound of claim 33 wherein at least one J is a sulfone.
51. (Original) The compound of claim 50 wherein Z is substituted or unsubstituted  $C_1$ - $C_{20}$  alkyl or substituted or unsubstituted  $C_5$ - $C_{20}$  aryl.
52. (Original) The compound of claim 33 wherein said internucleoside linking group is a phosphorus-containing internucleoside linking group.
53. (Original) The compound of claim 52 wherein said internucleoside linking group is a phosphodiester, a phosphorothioate or a phosphorodithioate.
54. (Original) The compound of claim 33 wherein m is from about 8 to about 30.

55. (Original) The compound of claim 33 wherein m is from about 15 to about 25.
56. (Original) The compound of claim 33 wherein each mm is 0.
57. (Original) The compound of claim 33 wherein n is 2.
58. (Original) The compound of claim 33 wherein each of said Bx is independently selected from the group consisting of adenine, guanine, thymine, cytosine, uracil, 5-methylcytosine (5-me-C), 5-hydroxymethyl cytosine, xanthine, hypoxanthine, 2-aminoadenine, alkyl derivatives of adenine and guanine, 2-thiouracil, 2-thiothymine, 2-thiocytosine, 5-halouracil, 5-halocytosine, 5-propynyl uracil, 5-propynyl cytosine, 6-azo uracil, 6-azo cytosine, 6-azo thymine, 5-uracil (pseudouracil), 4-thiouracil, 8-substituted adenines and guanines, 5-substituted uracils and cytosines, 7-methylguanine, 7-methyladenine, 8-azaguanine, 8-azaadenine, 7-deazaguanine, 7-deazaadenine, 3-deazaguanine and 3-deazaadenine.
59. (Original) The compound of claim 33 wherein each optionally protected sugar substituent groups is, independently, C<sub>1</sub>-C<sub>20</sub> alkyl, C<sub>2</sub>-C<sub>20</sub> alkenyl, C<sub>2</sub>-C<sub>20</sub> alkynyl, C<sub>5</sub>-C<sub>20</sub> aryl, -O-alkyl, -O-alkenyl, -O-alkynyl, -O-alkylamino, -O-alkylalkoxy, -O-alkylaminoalkyl, -O-alkyl imidazole, -OH, -SH, -S-alkyl, -S-alkenyl, -S-alkynyl, -N(H)-alkyl, -N(H)-alkenyl, -N(H)-alkynyl, -N(alkyl)<sub>2</sub>, -O-aryl, -S-aryl, -NH-aryl, -O-aralkyl, -S-aralkyl, -N(H)-aralkyl, phthalimido (attached at N), halogen, amino, keto (-C(=O)-R), carboxyl (-C(=O)OH), nitro (-NO<sub>2</sub>), nitroso (-N=O), cyano (-CN), trifluoromethyl (-CF<sub>3</sub>), trifluoromethoxy (-O-CF<sub>3</sub>), imidazole, azido (-N<sub>3</sub>), hydrazino (-N(H)-NH<sub>2</sub>), aminooxy (-O-NH<sub>2</sub>), isocyanato (-N=C=O), sulfoxide (-S(=O)-R), sulfone (-S(=O)<sub>2</sub>-R), disulfide (-S-S-R), silyl, heterocycle, carbocycle, intercalator, reporter group, conjugate, polyamine, polyamide, polyalkylene glycol, and polyethers of the formula (-O-alkyl)<sub>m</sub>, where m is 1 to about 10; wherein each R is, independently, hydrogen, a protecting group or substituted or unsubstituted alkyl, alkenyl, or alkynyl wherein said substituted alkyl, alkenyl, or alkynyl are substituted with haloalkyl, alkenyl, alkoxy, thioalkoxy, haloalkoxy, aryl groups as well as

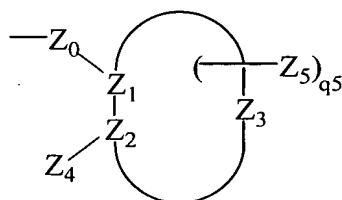
halogen, hydroxyl, amino, azido, carboxy, cyano, nitro, mercapto, sulfides, sulfones, and sulfoxides;

or each sugar substituent group has one of formula VI or VII:

wherein:



VI

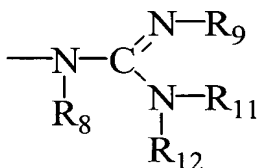


VII

$Z_0$  is O, S or NH;

J is a single bond, O or C(=O);

E is C<sub>1</sub>-C<sub>10</sub> alkyl, N(R<sub>5</sub>)(R<sub>6</sub>), N(R<sub>5</sub>)(R<sub>7</sub>), N=C(R<sub>5a</sub>)(R<sub>6a</sub>), N=C(R<sub>5a</sub>)(R<sub>7a</sub>) or has formula IX;



IX

each R<sub>8</sub>, R<sub>9</sub>, R<sub>11</sub> and R<sub>12</sub> is, independently, hydrogen, C(O)R<sub>13</sub>, substituted or unsubstituted C<sub>1</sub>-C<sub>10</sub> alkyl, substituted or unsubstituted C<sub>2</sub>-C<sub>10</sub> alkenyl, substituted or unsubstituted C<sub>2</sub>-C<sub>10</sub> alkynyl, alkylsulfonyl, arylsulfonyl, a chemical functional group or a conjugate group,

wherein the substituent groups are selected from hydroxyl, amino, alkoxy, carboxy, benzyl, phenyl, nitro, thiol, thioalkoxy, halogen, alkyl, aryl, alkenyl and alkynyl;

or optionally, R<sub>11</sub> and R<sub>12</sub>, together form a phthalimido moiety with the nitrogen atom to which they are attached;

each R<sub>13</sub> is, independently, substituted or unsubstituted C<sub>1</sub>-C<sub>10</sub> alkyl, trifluoromethyl, cyanoethoxy, methoxy, ethoxy, t-butoxy, allyloxy, 9-fluorenylmethoxy, 2-(trimethylsilyl)-ethoxy, 2,2,2-trichloroethoxy, benzyloxy, butyryl, iso-butyryl, phenyl or aryl;

R<sub>5</sub> is hydrogen, a nitrogen protecting group or -T-L,

R<sub>5a</sub> is hydrogen, a nitrogen protecting group or -T-L,

T is a bond or a linking moiety;

L is a chemical functional group, a conjugate group or a solid support material;

each  $R_6$  and  $R_7$  is, independently, H, a nitrogen protecting group, substituted or unsubstituted  $C_1$ - $C_{10}$  alkyl, substituted or unsubstituted  $C_2$ - $C_{10}$  alkenyl, substituted or unsubstituted  $C_2$ - $C_{10}$  alkynyl, wherein said substitution is hydroxyl, amino, alkoxy, carboxy, benzyl, phenyl, nitro, thiol, thioalkoxy, halogen, alkyl, aryl, alkenyl, alkynyl;  $NH_3^+$ ,  $N(R_{14})(R_{15})$ , guanidino or acyl where said acyl is an acid amide or an ester;

or  $R_6$  and  $R_7$ , together, are a nitrogen protecting group, are joined in a ring structure that optionally includes an additional heteroatom selected from N and O or are a chemical functional group;

each  $R_{14}$  and  $R_{15}$  is, independently, H,  $C_1$ - $C_{10}$  alkyl, a nitrogen protecting group, or  $R_{14}$  and  $R_{15}$ , together, are a nitrogen protecting group;

or  $R_{14}$  and  $R_{15}$  are joined in a ring structure that optionally includes an additional heteroatom selected from N and O;

$Z_4$  is OX, SX or  $N(X)_2$ ;

each X is, independently, H,  $C_1$ - $C_8$  alkyl,  $C_1$ - $C_8$  haloalkyl,  $C(=NH)N(H)R_{16}$ ,  $C(=O)N(H)R_{16}$  or  $OC(=O)N(H)R_{16}$ ;

$R_{16}$  is H or  $C_1$ - $C_8$  alkyl;

$Z_1$ ,  $Z_2$  and  $Z_3$  comprise a ring system having from about 4 to about 7 carbon atoms or having from about 3 to about 6 carbon atoms and 1 or 2 heteroatoms wherein said heteroatoms are selected from oxygen, nitrogen and sulfur and wherein said ring system is aliphatic, unsaturated aliphatic, aromatic, or saturated or unsaturated heterocyclic;

$Z_5$  is alkyl or haloalkyl having 1 to about 10 carbon atoms, alkenyl having 2 to about 10 carbon atoms, alkynyl having 2 to about 10 carbon atoms, aryl having 6 to about 14 carbon atoms,  $N(R_5)(R_6)$ , OR<sub>5</sub>, halo, SR<sub>5</sub> or CN;

each  $q_1$  is, independently, an integer from 1 to 10;

each  $q_2$  is, independently, 0 or 1;

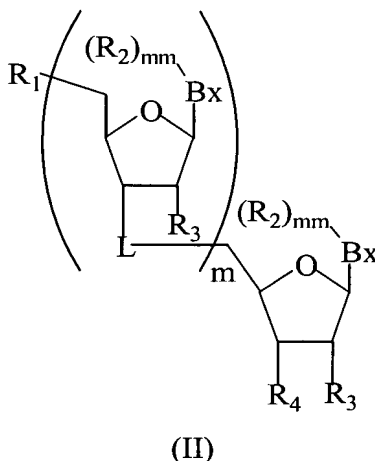
$q_3$  is 0 or an integer from 1 to 10;

$q_4$  is an integer from 1 to 10;

$q_5$  is from 0, 1 or 2; and

provided that when  $q_3$  is 0,  $q_4$  is greater than 1.

100. (New) A compound of formula II:



wherein:

each Bx is an optionally protected heterocyclic base moiety;

R<sub>1</sub> is hydrogen, hydroxyl, a protected hydroxyl, a nucleoside, a nucleotide, an oligonucleoside, an oligonucleotide or a group of formula I;

R<sub>4</sub> is hydrogen, hydroxyl, a protected hydroxyl, a nucleoside, a nucleotide, an oligonucleoside, an oligonucleotide or a group of formula I;

each R<sub>2</sub> is a group of formula I:



(I)

wherein:

each n is, independently, from 1 to about 10;

each J is, independently, a sulfonic acid ( $\text{—S(=O)}_2\text{OH}$ ), a sulfonate salt ( $\text{—S(=O)}_2\text{O}^-\text{X}^+$ ), a sulfoxide ( $\text{—S(=O)—Z}$ ), a sulfone ( $\text{—S(=O)}_2\text{—Z}$ ),  $\text{—SH}$ ,  $\text{—S—S—Z}$ , or a thiol ( $\text{—S—Z}$ );

each X<sup>+</sup> is a metal cation;

each Z is, independently, selected from the group consisting of C<sub>1</sub>–C<sub>20</sub> alkyl, C<sub>2</sub>–C<sub>20</sub> alkenyl, C<sub>2</sub>–C<sub>20</sub> alkynyl, C<sub>5</sub>–C<sub>20</sub> aryl and C<sub>5</sub>–C<sub>20</sub> aryl substituted C<sub>1</sub>–C<sub>20</sub> alkyl;

each R<sub>3</sub> is, independently, hydrogen, hydroxyl, a protected hydroxyl, an optionally protected sugar substituent group or a group of formula I;

**DOCKET NO.:** ISIS-4853  
**Application No.:** 10/058,740  
**Office Action Dated:** May 4, 2004

**PATENT**

L is an internucleoside linking group;  
m is from 3 to about 50; and  
each mm is, independently, 0 or 1;  
wherein at least one of said L is other than a phosphodiester internucleoside linkage and at least two of said R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub> and R<sub>4</sub> are groups of formula I.